REMARKS

A check for $450 for the requisite fee for a two-month extension of time accompanies this response. Any fees that may be due in connection with the filing of this paper or with this application may be charged to Deposit Account No. 06-1050. If a Petition for Extension of time is needed, this paper is to be considered such Petition. A DECLARATION pursuant to 37 C.F.R. § 1.78(c) accompanies this response.

Claims 1-25 are pending. Claims 41-55 are cancelled herein without prejudice or disclaimer. Applicant reserves the right to file a continuation application directed to the cancelled subject matter. Claims 1 and 15 are amended herein to recite "pharmaceutically acceptable salt thereof" in the last line of each claim. No new matter is added.

I. THE REJECTION OF CLAIMS 1-25 AND 41-55 UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 1-25 and 41-55 are rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly fails to describe the claimed subject matter in such a way as to enable one skilled in the art to make and use the claimed subject matter.

In order to advance prosecution to allowance, but without acquiescing to the rejection, claims 41-55 are cancelled herein without prejudice or disclaimer. Thus, the rejection as applied to claims 41-55 is moot. In addition, claims 1 and 15 are amended herein to delete the recitation "or prodrug," thereby obviating the rejection.

II. THE REJECTION OF CLAIMS 1-25 AND 41-55 UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 1-25 and 41-55 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for reasons discussed in turn below. Reconsideration is respectfully requested.

A. Claims 1-25

Claims 1-25 are rejected as indefinite because the term "prodrug" is allegedly indefinite because "specific prodrugs and a method of preparing them are not defined" in the specification. In order to advance prosecution to allowance, but without acquiescing to the rejection, claims 1 and 15 are amended herein to delete the recitation "or prodrug," thereby obviating the rejection.

B. Claims 41-55

In order to expedite prosecution, but without acquiescing to the rejection, claims 41-55 are cancelled herein without prejudice or disclaimer. Thus, the rejection as applied to claims 41-55 is moot.

REJECTION OF CLAIMS 1-25 AND 41-55 UNDER 35 U.S.C. §103(a)

Claims 1-25 and 41-55 are rejected under 35 U.S.C. §103(a) as being unpatentable over Jones *et al.* (U.S. Pat. No. 5,696,127) because Jones *et al.* allegedly teaches compounds of formulae V and VII having progesterone receptor agonist/antagonist activity for treating various conditions, and the allegedly most related compounds differ from the instant compounds only in that the have hydrogen as variable R^{14} (at position 7). The Examiner alleges that it would have been obvious to prepare the instant compounds because Jones *et al.* allegedly teaches that variable R^{14} also can be fluorine. This rejection is respectfully traversed.

ANALYSIS

1. Claims 41-55

Without acquiescing to the rejection, in order to advance prosecution of this application to allowance, claims 41-55 are cancelled herein without prejudice or disclaimer. Thus, the rejection as applied to claims 41-55 is moot.

2. Claims 1-25

At the time of invention of claims 1-25 of the instant application, the subject matter thereof was subject to an obligation of assignment to LIGAND PHARMACEUTICALS INCORPORATED. Attached hereto is a DECLARATION under 37 C.F.R. §1.78(c) attesting to the obligation of assignment of the instantly claimed subject matter to LIGAND PHARMACEUTICALS INCORPORATED. The attached DECLARATION attests that the inventors of the subject matter of the instant application were employees of LIGAND PHARMACEUTICALS INCORPORATED and were subject to an obligation of assignment to LIGAND PHARMACEUTICALS INCORPORATED at the time the experiments and work developing the subject matter disclosed and claimed in the instant application were performed. The attached DECLARATION also attests to the obligation of the inventors thereof to assign to LIGAND PHARMACEUTICALS INCORPORATED. The assignments of the inventors of U.S. Patent No. 5,696,127 evidencing assignment to LIGAND PHARMACEUTICALS INCORPORATED were executed on June 2, 1995, and were recorded June 5, 1995 on reel 007551, frame 0595. Therefore, at the time of invention of claims 1-25 of the instant application, the subject matter claimed in the instant application and the subject matter of U.S. Patent No. 5,696,127 were commonly owned by or subject to an obligation of assignment to LIGAND PHARMACEUTICALS INCORPORATED. Thus, Jones *et al.* (U.S. Pat. No. 5,696,127) is not prior art.

OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTIONS

1. U.S. Patent No. 5,696,127 – Jones *et al.*

Claims 1-25 and 41-55 are rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-5, 7-15, 17, 19-22, 24-28, 30-33 and 35 of U.S. Patent No. 5,696,127 (hereinafter the '127 patent). The Examiner alleges that, although the conflicting claims are not identical, they are not patently distinct, because the instant compounds of formula (I), pharmaceutical compounds containing these compounds and methods of using these compounds are encompassed by compounds of formula (V) of the '127 patent, pharmaceutical compounds containing these compounds and methods of using these compounds when R^{12} and R^{14} of formula (V) of the '127 patent are F. This rejection is respectfully traversed.

Relevant Law

The disclosure of a patent cited in support of a double patenting rejection cannot be used as though it were prior art even where the disclosure is found in the claims. Obvious-type double patenting signifies that the difference between a first-patented invention and its variant involves only an unpatentable difference, such that grant of the second patent would extend the right of exclusivity conferred by the first patent. Comparison can be made only with what invention is claimed in the earlier patent, paying careful attention to the rules of claim interpretation to determine what invention a claim defines and not looking to the claim for anything that happens to be mentioned in it as though it were a prior art reference. A fundamental rule of claim construction requires that what is claimed is what is defined by the claims taken as a whole, and every claim limitation (each step) is material. *General Foods Corp. v. Studiengesellschaft Kohle mbH*, 23 USPQ 1839 (Fed. Cir. 1992).

Double-patenting has not been found in instances in which the claims at issue do not embrace the prior patent compounds and/or the claims in the prior patent do not suggest any modification that would have produced the claimed compounds in the patent or application at issue (see, *e.g., Ortho Pharmaceutical Corp v. Smith*, 22 USPQ2d 1119 (Fed. Cir. 1992), in which obvious-type double patenting was not found in an instance in which the claims at issue were directed to compounds that did not encompass, structurally, the compounds claimed in the prior patents, and the compounds claimed in the prior patents did not suggest a modification of those compounds to produce compounds of the claims at issue.

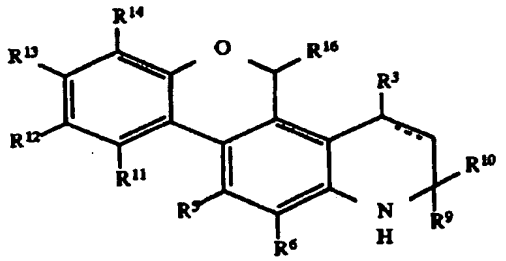
The test is whether the right of exclusivity for the species covered by the claimed subject matter in the application at issue would extend coverage for that species in the issued

patent. This can only be determined by applying principles of claim interpretation to the first patent to determine what is covered by the claims, not by using the prior patented claims as prior art. Thus, obvious-type patenting does not exist if the claims at issue do not encompass the claimed subject matter in the issued patent, and, the claims in the issued patent do not suggest a modification to produce the claims in the subject application.

Claims 1-5, 7-15, 17, 19-22, 24-28, 30-33 and 35 of Jones *et al.*, U.S. 5,696,127

Independent Claim 1 of U.S. Pat. No. 5,696,127 recites:

1. A compound of the formula:



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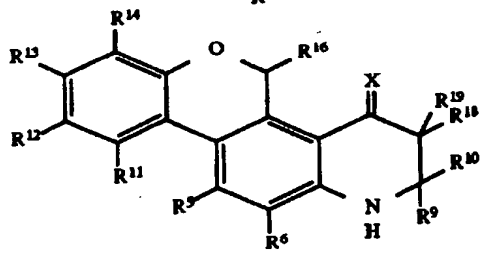

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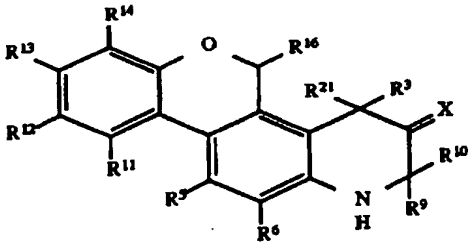

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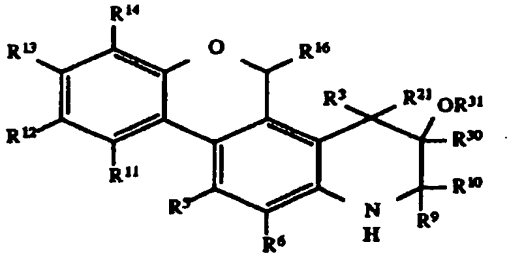

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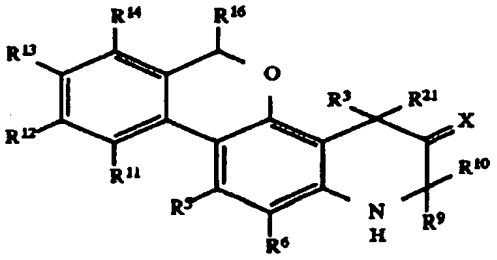

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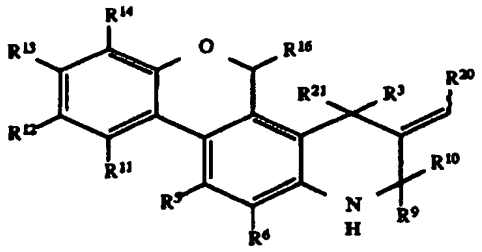

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wherein:

R^2 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl;

R^3 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, hydroxymethyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl;

R^5 through R^6 each independently are hydrogen, F, Cl, Br, I, NO_2, CO_2H, CO_2R^2, COR^2, CN, CF_3, CH_2OH, a C_1-C_4 alkyl or perfluoroalkyl, OR^2, SR^2, $S(O)R^2$, SO_2R^2, SO_3H, $S(NR^2R^7)R^2$, $S(O)(NR^2R^7)R^2$, NR^2R^7, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl, where R^2 has the definition given above, R^7 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, aryl, heteroaryl, optionally substituted allyl or arylmethyl, OR^8 or NHR^8, where R^8 is hydrogen, a C_1-C_6 alkyl or perfluoroalkyl, aryl, heteroaryl, optionally substituted allyl or arylmethyl, SO_2R^2 or $S(O)R^2$;

R^9 and R^{10} each independently are hydrogen, a C_1-C_6 alkyl or perfluoroalkyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl, or R^9 and R^{10} taken together can form a three- to seven-membered ring optionally substituted with hydrogen, F, OR^2, or NR^2R^7, where R^2 and R^7 have the definitions given above;

R^{11} through R^{14} each independently are hydrogen, F, Cl, Br, I, NO_2, CO_2H, CO_2R^2, COR^2, CN, CF_3, CH_2OH, a C_1-C_4 alkyl or perfluoroalkyl, OR^2, SR^2, $S(O)R^2$, SO_2R^2, SO_3H, $S(NR^2R^7)R^2$, $S(O)(NR^2R^7)R^2$, NR^2R^7, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl, where R^2, R^7 and R^8 have the definitions given above;

X is CH_2, O, S or NR^7, where R^7 has the definition given above;

R^{16} is hydrogen, OH, OR^{17}, SR^{17}, NR^2R^7, optionally substituted allyl, arylmethyl, alkynyl, alkenyl, aryl, heteroaryl or C_1-C_{10} alkyl, where R^{17} is a C_1-C_{10} alkyl or perfluoroalkyl, or is an optionally substituted allyl, arylmethyl, aryl or heteroaryl, and where R^2 and R^7 have the definitions given above;

R^{18} and R^{19} each independently are hydrogen, a C_1-C_6 alkyl or perfluoroalkyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl, or R^{18} and R^{19} taken together can form a three- to seven-membered ring optionally substituted with hydrogen, F, OR^2, or NR^7R^8, where R^2, R^7 and R^8 have the definitions given above;

R^{20} is a C_1-C_6 alkyl or an optionally substituted allyl, arylmethyl, alkenyl, aryl or heteroaryl;

R^{21} is hydrogen, a C_1-C_4 alkyl or optionally substituted allyl, arylmethyl, aryl or heteroaryl;

R^{22} is hydrogen, a C_1-C_4 alkyl, F, Cl, Br, I, OR^2, NR^2R^7 or SR^2, where R^2 and R^7 have the definitions given above;

R^{30} and R^{31} each independently are hydrogen, a C_1-C_6 alkyl or an optionally substituted allyl, arylmethyl, aryl or heteroaryl, or R^{30} and R^{31} taken together can form a three- to seven-membered ring optionally substituted with hydrogen, F, Cl, OR^2 or NR^2R^7, where R^2 and R^7 have the definitions given above;

the wavy line in the compounds of formula XVI represent an olefin bond in either the

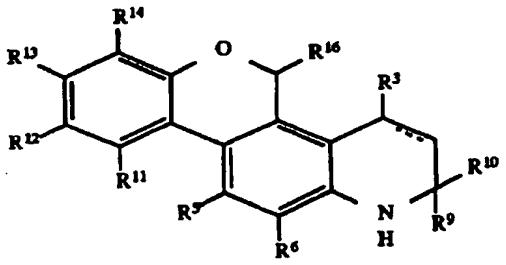
cis or trans configuration; and

the dotted lines in the structures depict optional double bonds.

Claims 2-5, 7-15 and 17 depend from claim 1 and are directed to various embodiments thereof.

Independent Claim 19 recites:

A pharmaceutical composition that modulates progesterone receptor or having glucocorticoid receptor antagonist activity, comprising an effective amount of a progesterone receptor modulating or glucocorticoid receptor antagonist compound of the formula:



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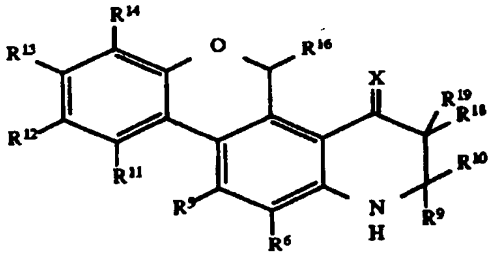

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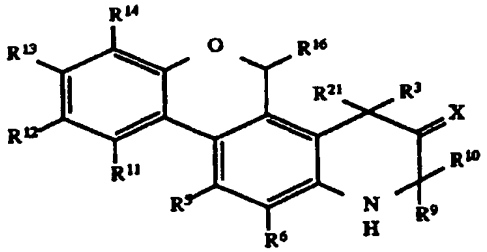

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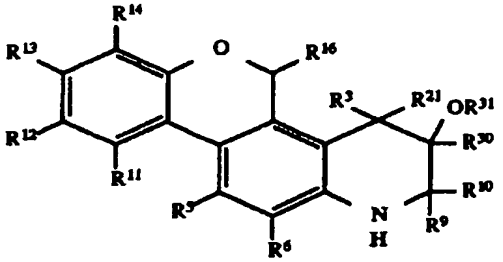

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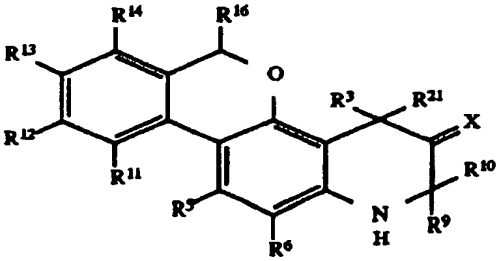

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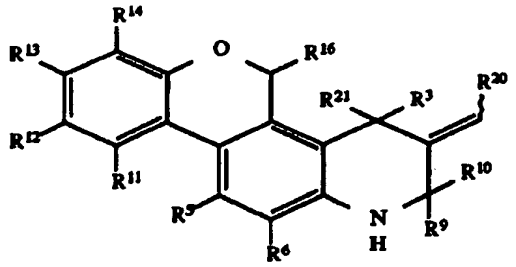
or  (XVI)

wherein:

R^2 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl;

R^3 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, hydroxymethyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl;

R^5 through R^6 each independently are hydrogen, F, Cl, Br, I, NO_2, CO_2H, CO_2R^2, COR^2, CN, CF_3, CH_2OH, a C_1-C_4 alkyl or perfluoroalkyl, OR^2, SR^2, $S(O)R^2$, SO_2R^2, SO_3H, $S(NR^2R^7)R^2$, $S(O)(NR^2R^7)R^2$, NR^2R^7, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl, where R^2 has the definition given above, R^7 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, aryl, heteroaryl, optionally substituted allyl or arylmethyl, OR^8 or NHR^8, where R^8 is hydrogen, a C_1-C_6 alkyl or perfluoroalkyl, aryl, heteroaryl, optionally substituted allyl or arylmethyl, SO_2R^2 or $S(O)R^2$;

R^9 and R^{10} each independently are hydrogen, a C_1-C_6 alkyl or perfluoroalkyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl, or R^9 and R^{10} taken together can form a three- to seven-membered ring optionally substituted with hydrogen, F, OR^2, or NR^2R^7, where R^2 and R^7 have the definitions given above;

R^{11} through R^{14} each independently are hydrogen, F, Cl, Br, I, NO_2, CO_2H, CO_2R^2, COR^2, CN, CF_3, CH_2OH, a C_1-C_4 alkyl or perfluoroalkyl, OR^2, SR^2, $S(O)R^2$, SO_2R^2, SO_3H, $S(NR^2R^7)R^2$, $S(O)(NR^2R^7)R^2$, NR^2R^7, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl, where R^2, R^7 and R^8 have the definitions given above;

X is CH_2, O, S or NR^7, where R^7 has the definition given above;

R^{16} is hydrogen, OH, OR^{17}, SR^{17}, NR^2R^7, optionally substituted allyl, arylmethyl, alkynyl, alkenyl, aryl, heteroaryl or C_1-C_{10} alkyl, where R^{17} is a C_1-C_{10} alkyl or perfluoroalkyl, or is an optionally substituted allyl, arylmethyl, aryl or heteroaryl, and where R^2 and R^7 have the definitions given above;

R^{18} and R^{19} each independently are hydrogen, a C_1-C_6 alkyl or perfluoroalkyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl, or R^{18} and R^{19} taken together can form a three- to seven-membered ring optionally substituted with hydrogen, F, OR^2, or NR^7R^8, where R^2, R^7 and R^8 have the definitions given above;

R^{20} is a C_1-C_6 alkyl or an optionally substituted allyl, arylmethyl, alkenyl, aryl or heteroaryl;

R^{21} is hydrogen, a C_1-C_4 alkyl or optionally substituted allyl, arylmethyl, aryl or heteroaryl;

R^{22} is hydrogen, a C_1-C_4 alkyl, F, Cl, Br, I, OR^2, NR^2R^7 or SR^2, where R^2 and R^7 have the definitions given above;

R^{30} and R^{31} each independently are hydrogen, a C_1-C_6 alkyl or an optionally substituted allyl, arylmethyl, aryl or heteroaryl, or R^{30} and R^{31} taken together can form a three- to seven-membered ring optionally substituted with hydrogen, F, Cl, OR^2 or NR^2R^7, where R^2 and R^7 have the definitions given above;

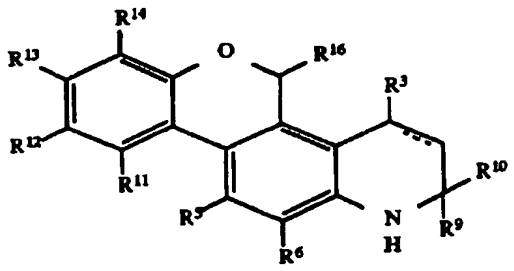
the wavy line in the compounds of formula XVI represent an olefin bond in either the cis or trans configuration; the dotted lines in the structures depict optional double bonds; and

a pharmaceutically acceptable carrier.

Claims 20-22 and 24-28 depend from claim 19 and are directed to various embodiments thereof.

Independent Claim 30 recites:

A method of treating a patient requiring progesterone receptor therapy or a glucocorticoid receptor antagonist comprising administering to a patient an effective amount of a progesterone receptor modulating or a glucocorticoid receptor antagonist compound having the formula:



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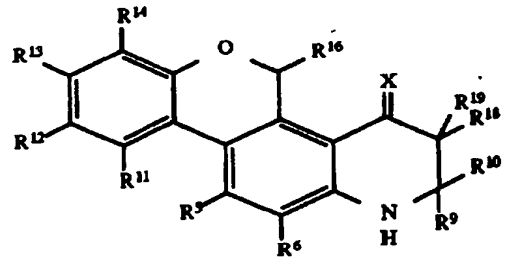

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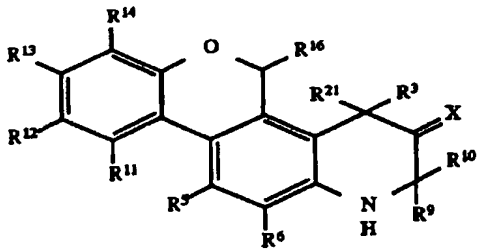

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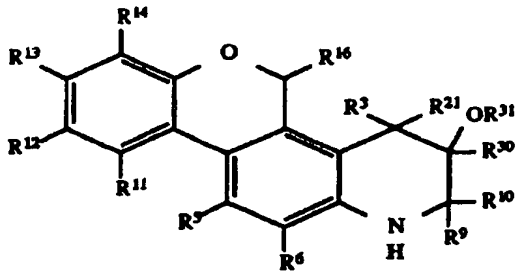

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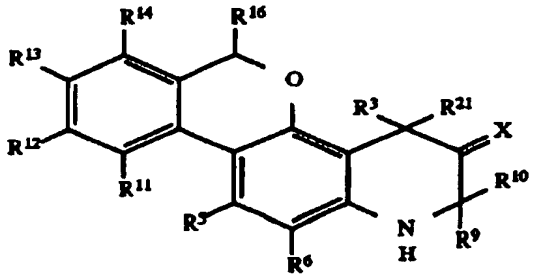

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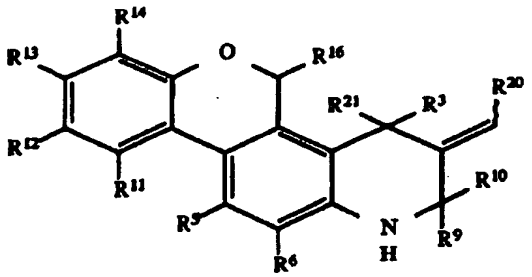


(XVI)

wherein:

R^2 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl;

R^3 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, hydroxymethyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl;

R^5 through R^6 each independently are hydrogen, F, Cl, Br, I, NO_2, CO_2H, CO_2R^2, COR^2, CN, CF_3, CH_2OH, a C_1-C_4 alkyl or perfluoroalkyl, OR^2, SR^2, $S(O)R^2$, SO_2R^2, SO_3H, $S(NR^2R^7)R^2$, $S(O)(NR^2R^7)R^2$, NR^2R^7, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl, where R^2 has the definition given above, R^7 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, aryl, heteroaryl, optionally substituted allyl or arylmethyl, OR^8 or NHR^8, where R^8 is hydrogen, a C_1-C_6 alkyl or perfluoroalkyl, aryl, heteroaryl, optionally substituted allyl or arylmethyl, SO_2R^2 or $S(O)R^2$;

R^9 and R^{10} each independently are hydrogen, a C_1-C_6 alkyl or perfluoroalkyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl, or R^9 and R^{10} taken together can form a three- to seven-membered ring optionally substituted with hydrogen, F, OR^2, or NR^2R^7, where R^2 and R^7 have the definitions given above;

R^{11} through R^{14} each independently are hydrogen, F, Cl, Br, I, NO_2, CO_2H, CO_2R^2, COR^2, CN, CF_3, CH_2OH, a C_1-C_4 alkyl or perfluoroalkyl, OR^2, SR^2, $S(O)R^2$, SO_2R^2, SO_3H, $S(NR^2R^7)R^2$, $S(O)(NR^2R^7)R^2$, NR^2R^7, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl, where R^2, R^7 and R^8 have the definitions given above;

X is CH_2,O, S or NR^7, where R^7 has the definition given above;

R^{16} is hydrogen, OH, OR^{17}, SR^{17}, NR^2R^7, optionally substituted allyl, arylmethyl, alkynyl, alkenyl, aryl, heteroaryl or C_1-C_{10} alkyl, where R^{17} is a C_1-C_{10} alkyl or perfluoroalkyl, or is an optionally substituted allyl, arylmethyl, aryl or heteroaryl, and where R^2 and R^7 have the definitions given above;

R^{18} and R^{19} each independently are hydrogen, a C_1-C_6 alkyl or perfluoroalkyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl, or R^{18} and R^{19} taken together can form a three- to seven-membered ring optionally substituted with hydrogen, F, OR^2, or NR^7R^8, where R^2, R^7 and R^8 have the definitions given above;

R^{20} is a C_1-C_6 alkyl or an optionally substituted allyl, arylmethyl, alkenyl, aryl or heteroaryl;

R^{21} is hydrogen, a C_1-C_4 alkyl or optionally substituted allyl, arylmethyl, aryl or heteroaryl;

R^{22} is hydrogen, a C_1-C_4 alkyl, F, Cl, Br, I, OR^2, NR^2R^7 or SR^2, where R^2 and R^7 have the definitions given above;

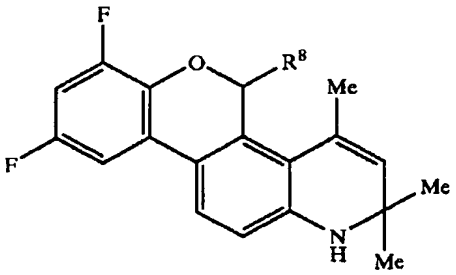
R^{30} and R^{31} each independently are hydrogen, a C_1-C_6 alkyl or an optionally substituted allyl, arylmethyl, aryl or heteroaryl, or R^{30} and R^{31} taken together can form a three- to seven-membered ring optionally substituted with hydrogen, F, Cl, OR^2 or NR^2R^7, where R^2 and R^7 have the definitions given above;

the wavy line in the compounds of formula XVI represent an olefin bond in either the *cis* or *trans* configuration; and the dotted lines in the structures depict optional double bonds.

Claims 31-33 and 35 depend from claim 30 and are directed to embodiments thereof.

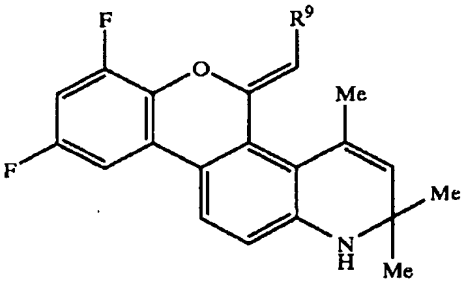
The Independent Rejected Claims in This Application

Independent claim 1 recites a compound of the formula:



(I)

or



(II)

wherein:

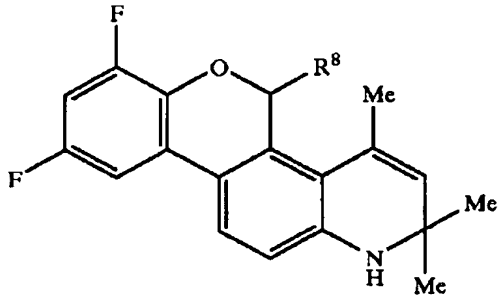
R^8 is selected from the group of C_1-C_{12} alkyl, C_1-C_{12} heteroalkyl, C_1-C_{12} haloalkyl, C_2-C_{12} alkenyl, C_2-C_{12} heteroalkenyl, C_2-C_{12} haloalkenyl, C_2-C_{12} alkynyl, C_2-C_{12} heteroalkynyl, C_2-C_{12} haloalkynyl, aryl and heteroaryl, optionally substituted with one or more substituents independently selected from the group of hydrogen, C_1-C_4 alkyl, F, Cl, Br, I, CN, NO_2, NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SCH_3, OH, OCH_3, OCF_3, CF_3, $C(O)CH_3$, $CO2CH_3$, $C(O)NH_2$, OR^{10}, SR^{10}, and $NR^{10}R^{11}$;

R^9 is selected from the group of hydrogen, F, Cl, Br, I, CN, C_1-C_8 alkyl, C_1-C_8 heteroalkyl, C_1-C_8 haloalkyl, C_2-C_8 alkenyl or cycloalkenyl, C_2-C_8 heteroalkenyl, C_2-C_8 haloalkenyl, C_2-C_8 alkynyl, C_2-C_8 heteroalkynyl, C_2-C_8 haloalkynyl, aryl and heteroaryl, optionally substituted with one or more substituents independently selected from the group of hydrogen, C_1-C_4 alkyl, F, Cl, Br, I, CN, NO_2, NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SCH_3, OH, OCH_3, OCF_3, CF_3, $C(O)CH_3$, CO_2CH_3, $C(O)NH_2$, OR^{10}, SR^{10}, and $NR^{10}R^{11}$;

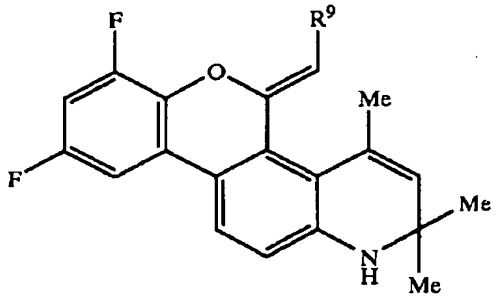
R^{10} and R^{11} each independently is hydrogen, or C_1-C_4 alkyl;

or a pharmaceutically acceptable salt thereof.

Independent Claim 15 recites a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of formula:



(I)

or 

(II)

wherein:

R^8 is selected from the group of C_1-C_{12} alkyl, C_1-C_{12} heteroalkyl, C_1-C_{12} haloalkyl, C_2-C_{12} alkenyl, C_2-C_{12} heteroalkenyl, C_2-C_{12} haloalkenyl, C_2-C_{12} alkynyl, C_2-C_{12} heteroalkynyl, C_2-C_{12} haloalkynyl, aryl and heteroaryl optionally substituted with one or more substituents independently selected from the group of hydrogen, C_1-C_4 alkyl, F, Cl, Br, I, CN, NO_2, NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SCH_3, OH, OCH_3, OCF_3, CF_3, $C(O)CH_3$, CO_2CH_3, $C(O)NH_2$, OR^{10}, SR^{10}, and $NR^{10}R^{11}$;

R^9 is selected from the group of hydrogen, F, Cl, Br, I, CN, C_1-C_8 alkyl, C_1-C_8 heteroalkyl, C_1-C_8 haloalkyl, C_2-C_8 alkenyl or cycloalkenyl, C_2-C_8 heteroalkenyl, C_2-C_8 haloalkenyl, C_2-C_8 alkynyl, C_2-C_8 heteroalkynyl, C_2-C_8 haloalkynyl, aryl and heteroaryl optionally substituted with one or more substituents independently selected from the group of hydrogen, C_1-C_4 alkyl, F, Cl, Br, I, CN, NO_2, NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SCH_3, OH, OCH_3, OCF_3, CF_3, $C(O)CH_3$, CO_2CH_3, $C(O)NH_2$, OR^{10}, SR^{10}, and $NR^{10}R^{11}$; and

R^{10} and R^{11} each independently is hydrogen, or C_1-C_4 alkyl;

or a pharmaceutically acceptable salt thereof.

ANALYSIS

As directed to claims 41-55, the rejection is moot in light of the cancellation of claims 41-55 herein. As directed to claims 1-25, Applicant respectfully traverses the rejection.

The Examiner alleges that the instant compounds of Formula I and pharmaceutical compositions including compounds of Formula I are encompassed by compounds of Formula V of U.S. Patent No. 5,696,127 (the '127 patent) and pharmaceutical compositions including compounds of Formula V when R^{12} and R^{14} of Formula V of the '127 patent are fluorine. Applicant respectfully submits that the test for obviousness-type double patenting is whether the claims at issue embrace the prior patent compounds, **not** whether the compounds of the prior patent encompass the compounds of the instant claims. In this instance, the claims at issue do not encompass the claims of the '127 patent. Applicant respectfully submits that, even though there is overlap, there are compounds of Formula V of the '127 patent that are not encompassed by the instant claims.

Independent claim 1 in the '127 patent recites compounds of Formulae V, VI, VIII, XIV, XV or XVI, having various substituents as defined in the claim. For example, the compounds of claim 1 of the '127 patent include substituents at position 5 represented by

R^{16}, which is selected from among hydrogen, OH, OR^{17}, SR^{17}, NR^2R^7, optionally substituted allyl, arylmethyl, alkynyl, alkenyl, aryl, heteroaryl or C_1-C_{10} alkyl, where R^{17} is a C_1-C_{10} alkyl or perfluoroalkyl, or is an optionally substituted allyl, arylmethyl, aryl or heteroaryl, R^2 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl; and R^7 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, aryl, heteroaryl, optionally substituted allyl or arylmethyl, OR^8 or NHR^8, where R^8 is hydrogen, a C_1-C_6 alkyl or perfluoroalkyl, aryl, heteroaryl, optionally substituted allyl or arylmethyl, SO_2R^2 or $S(O)R^2$.

Independent claim 1 in the instant application recites compounds of Formulae I or II, having a double bond between positions 3 and 4, and having as substituents 2 methyl groups at position 2, a methyl substituent at position 4, a fluorine substituent at position 7 and position 9, hydrogen substituents at positions 8 and 10-12 and substituents at position 5 represented by R^8, which is selected from among C_1-C_{12} alkyl, C_1-C_{12} heteroalkyl, C_1-C_{12} haloalkyl, C_2-C_{12} alkenyl, C_2-C_{12} heteroalkenyl, C_2-C_{12} haloalkenyl, C_2-C_{12} alkynyl, C_2-C_{12} heteroalkynyl, C_2-C_{12} haloalkynyl, aryl and heteroaryl optionally substituted with one or more substituents independently selected from the group of hydrogen, C_1-C_4 alkyl, F, Cl, Br, I, CN, NO_2, NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SCH_3, OH, OCH_3, OCF_3, CF_3, $C(O)CH_3$, CO_2CH_3, $C(O)NH_2$, OR^{10}, SR^{10}, and $NR^{10}R^{11}$, where R^{10} and R^{11} each independently is hydrogen or C_1-C_4 alkyl.

Thus, when comparing the compounds as instantly claimed to the compounds claimed in the '127 patent, there are compounds of Formula V of the '127 patent that are not encompassed by the instant claims. For example, the claims of the '127 patent include compounds with substituents at position 5, such as, *e.g.*, hydrogen, -OH, OR^{17}, SR^{17}, NR^2R^7 and optionally substituted allyl, that the instant claims do not recite. Therefore, the instant claims do not encompass the issued claims of the '127 patent.

Furthermore, the issued patent claims do not suggest a modification that would result in the instant claims. None of claims 1-5, 7-15, 17, 19-22, 24-28, 30-33 and 35 of U.S. Patent No. 5,696,127 suggest a compound of Formula V of the '127 patent with fluorine at position 7 and position 9. None of claims 1-5, 7-15, 17, 19-22, 24-28, 30-33 and 35 of U.S. Patent No. 5,696,127 suggest a compound of Formula V of the '127 patent with a double bond between positions 3 and 4 and substituted at positions 2 and 4 with methyl groups, at position 7 and 9 with fluorine, and at positions 8 and 10-12 with hydrogen. Thus, because the compounds of instant claim 1 do not encompass the compounds of claim 1 of the '127 patent and none of the claims in the '127 patent suggest any modification that would have produced the claimed

compounds in the instant application, as between instant claim 1 and claim 1 of the '127 patent, obviousness-type double patenting does not exist.

Instant claims 2-14 ultimately depend from claim 1 and include every limitation thereof. Independent claim 15 is directed to a pharmaceutical composition that includes a pharmaceutically acceptable carrier and a compound of Formulae I or II, as discussed above. Claims 16-25 depend from claim 15 and are directed to various embodiments thereof.

Therefore, because none of the instant claims encompass the claims of the '127 patent and none of the claims in the '127 patent suggest any modification that would have produced the claimed compounds in the instant application nor pharmaceutical compositions that include such compounds, as between claims 1-5, 7-15, 17, 19-22, 24-28, 30-33 and 35 in U.S. Patent No. 5,696,127 and pending claims 1-25, obviousness-type double patenting does not exist.

2. U.S. Patent No. 5,693,646 – Jones *et al.*

Claims 1-25 and 41-55 are rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-27 of U.S. Patent No. 5,693,646 (hereinafter the '646 patent). The Examiner alleges that, although the conflicting claims are not identical, they are not patently distinct, because the instant compounds of Formula II, pharmaceutical compounds containing these compounds and methods of using these compounds are encompassed by compounds of Formula VII of the '646 patent, pharmaceutical compounds containing these compounds and methods of using these compounds when R^{12} and R^{14} of Formula VII of the '646 patent are F. This rejection is respectfully traversed.

Relevant Law

See related section above.

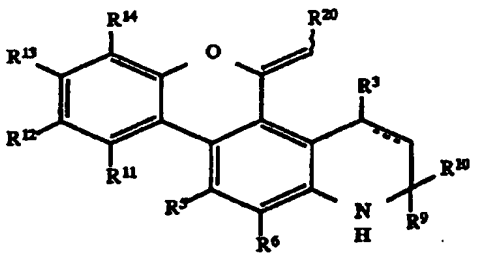
Rejected Independent Claims in This Application

See related section above.

Claims 1-27 of Jones *et al.*, U.S. 5,693,646

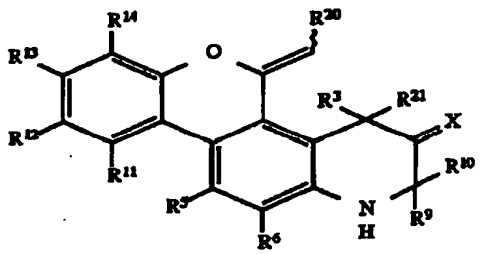
Independent Claim 1 of U.S. Pat. No. 5,693,646 recites:

1. A compound of the formula:



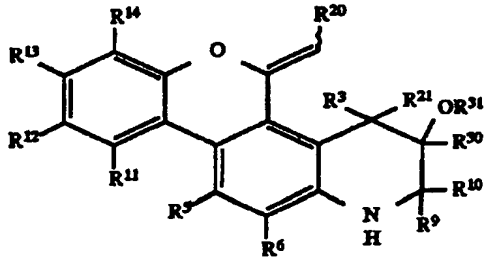
(VII)

or



(XII)

or



(XIII)

wherein:

R^2 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, aryl, heteroaryl, or optionally substituted allyl, arylmethyl, alkynyl or alkenyl;

R^3 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, hydroxymethyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl;

R^5 through R^6 each independently are hydrogen, F, Cl, Br, I, NO_2, CO_2H, CO_2R^2, COR^2, CN, CF_3, CH_2 OH, a C_1-C_4 alkyl or perfluoroalkyl, OR^2, SR^2, $S(O)R^2$, SO_2R^2, SO_3H, $S(NR^2R^7)R^2$, $S(O)(NR^2R^7)R^2$, NR^2R^7, aryl, heteroaryl or optionally substituted allyl, arylmethyl alkynyl or alkenyl, where R^2 has the definition given above, R^7 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, aryl, heteroaryl, optionally substituted allyl, arylmethyl, or OR^8 or NHR^8, where R^8 is hydrogen, a C_1-C_6 alkyl or perfluoroalkyl, aryl, heteroaryl, optionally substituted allyl or arylmethyl, SO_2R^2 or $S(O)R^2$;

R^9 and R^{10} each independently are hydrogen, a C_1-C_6 alkyl or perfluoroalkyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl, or R^9 and R^{10} taken together can form a three- to seven-membered ring optionally substituted with hydrogen, F, OR^2, or NR^2R^7, where R^2 and R^7 have the definitions given above;

R^{11} through R^{14} each independently are hydrogen, F, Cl, Br, I, NO_2, CO_2H, CO_2R^2, COR^2, CN, CF_3, CH_2OH, a C_1-C_4 alkyl or perfluoroalkyl, OR^2, SR^2, $S(O)R^2$, SO_2R^2, SO_3H, $S(NR^2R^7)R^2$, $S(O)(NR^2R^7)R^2$, NR^2R^7, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl, where R^2, R^7 and R^8 have the definitions given above;

X is CH_2, O, S or NR^7, where R^7 has the definition given above;

R^{20} is a C_1-C_6 alkyl or an optionally substituted allyl, arylmethyl, alkenyl, aryl or heteroaryl;

R^{21} is hydrogen, a C_1-C_4 alkyl or optionally substituted allyl, arylmethyl, aryl or heteroaryl;

R^{30} and R^{31} each independently are hydrogen, a C_1-C_6 alkyl or an optionally substituted allyl, arylmethyl, aryl or heteroaryl, or R^{30} and R^{31} taken together can form a three- to seven-membered ring optionally substituted with hydrogen, F, Cl, OR^2 or NR^2R^7, where R^2 and R^7 have the definitions given above;

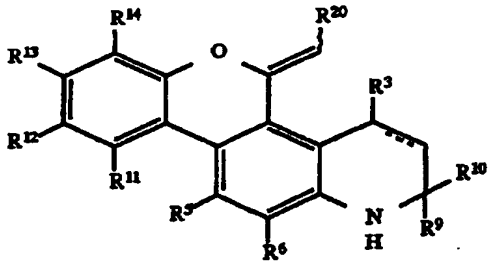
the wavy line in the compounds of formulas VII, XII and XIII represent an olefin bond in either the cis or trans configuration; and

the dotted lines in the structures depict optional double bonds.

Claims 2-13 depend from claim 1 and are directed to various embodiments thereof.

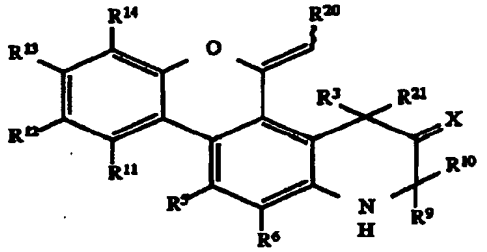
Independent Claim 14 recites:

A pharmaceutical composition which modulates progesterone receptor activity comprising an effective amount of a progesterone receptor modulating compound of the formula:



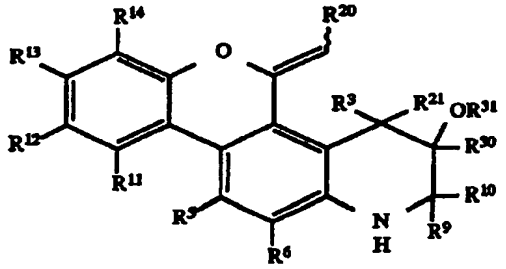
(VII)

or



(XII)

or



(XIII)

wherein:

R^2 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, aryl, heteroaryl, or optionally substituted allyl, arylmethyl, alkynyl or alkenyl;

R^3 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, hydroxymethyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl;

R^5 through R^6 each independently are hydrogen, F, Cl, Br, I, NO_2, CO_2H, CO_2R^2, COR^2, CN, CF_3, CH_2 OH, a C_1-C_4 alkyl or perfluoroalkyl, OR^2, SR^2, $S(O)R^2$, SO_2R^2, SO_3H, $S(NR^2R^7)R^2$, $S(O)(NR^2R^7)R^2$, NR^2R^7, aryl, heteroaryl or optionally substituted allyl, arylmethyl alkynyl or alkenyl, where R^2 has the definition given above, R^7 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, aryl, heteroaryl, optionally substituted allyl, arylmethyl, or OR^8 or NHR^8, where R^8 is hydrogen, a C_1-C_6 alkyl or perfluoroalkyl, aryl, heteroaryl, optionally substituted allyl or arylmethyl, SO_2R^2 or $S(O)R^2$;

R^9 and R^{10} each independently are hydrogen, a C_1-C_6 alkyl or perfluoroalkyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl, or R^9 and R^{10} taken together can form a three- to seven-membered ring optionally substituted with hydrogen, F, OR^2, or NR^2R^7, where R^2 and R^7 have the definitions given above;

R^{11} through R^{14} each independently are hydrogen, F, Cl, Br, I, NO_2, CO_2H, CO_2 R^2, COR^2, CN, CF_3, CH_2OH, a C_1-C_4 alkyl or perfluoroalkyl, OR^2, SR^2, $S(O)R^2$, SO_2R^2, SO_3H, $S(NR^2R^7)R^2$, $S(O)(NR^2R^7)R^2$, NR^2R^7, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl, where R^2, R^7 and R^8 have the definitions given above;

X is CH_2, O, S or NR^7, where R^7 has the definition given above;

R^{20} is a C_1-C_6 alkyl or an optionally substituted allyl, arylmethyl, alkenyl, aryl or heteroaryl;

R^{21} is hydrogen, a C_1-C_4 alkyl or optionally substituted allyl, arylmethyl, aryl or heteroaryl;

R^{30} and R^{31} each independently are hydrogen, a C_1-C_6 alkyl or an optionally substituted allyl, arylmethyl, aryl or heteroaryl, or R^{30} and R^{31} taken together can form a three- to seven-membered ring optionally substituted with hydrogen, F, Cl, OR^2 or NR^2R^7, where R^2 and R^7 have the definitions given above;

the wavy line in the compounds of formulas VII, XII and XIII represent an olefin bond in either the cis or trans configuration;

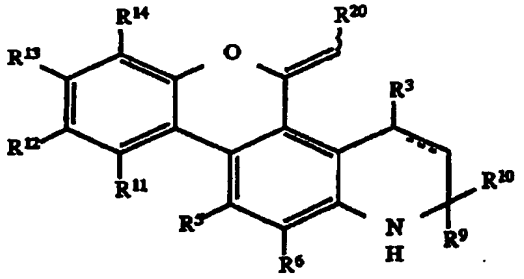
the dotted lines in the structures depict optional double bonds; and

a pharmaceutically acceptable carrier.

Claims 15 – 22 depend from claim 14 and are directed to various embodiments thereof.

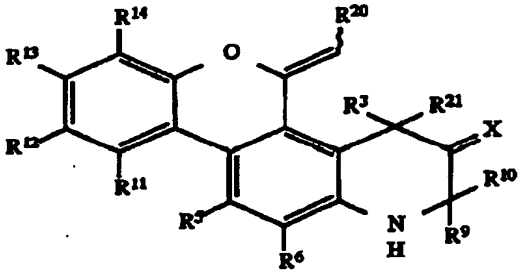
Independent Claim 23 recites:

A method of treating a patient requiring progesterone receptor therapy comprising administering to a patient an effective amount of a progesterone receptor modulating compound having the formula:



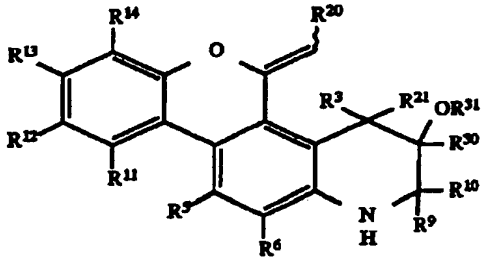
(VII)

or



(XII)

or



(XIII)

wherein:

R^2 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, aryl, heteroaryl, or optionally substituted allyl, arylmethyl, alkynyl or alkenyl;

R^3 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, hydroxymethyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl;

R^5 through R^6 each independently are hydrogen, F, Cl, Br, I, NO_2, CO_2H, CO_2R^2, COR^2, CN, CF_3, CH_2 OH, a C_1-C_4 alkyl or perfluoroalkyl, OR^2, SR^2, $S(O)R^2$, SO_2R^2, SO_3H, $S(NR^2R^7)R^2$, $S(O)(NR^2R^7)R^2$, NR^2R^7, aryl, heteroaryl or optionally substituted allyl, arylmethyl alkynyl or alkenyl, where R^2 has the definition given above, R^7 is hydrogen, a C_1-C_4 alkyl or perfluoroalkyl, aryl, heteroaryl, optionally substituted allyl, arylmethyl, or OR^8 or NHR^8, where R^8 is hydrogen, a C_1-C_6 alkyl or perfluoroalkyl, aryl, heteroaryl, optionally substituted allyl or arylmethyl, SO_2R^2 or $S(O)R^2$;

R^9 and R^{10} each independently are hydrogen, a C_1-C_6 alkyl or perfluoroalkyl, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl, or R^9 and R^{10} taken together can form a three- to seven-membered ring optionally substituted with hydrogen, F, OR^2, or NR^2R^7, where R^2 and R^7 have the definitions given above;

R^{11} through R^{14} each independently are hydrogen, F, Cl, Br, I, NO_2, CO_2H, CO_2 R^2, COR^2, CN, CF_3, CH_2OH, a C_1-C_4 alkyl or perfluoroalkyl, OR^2, SR^2, $S(O)R^2$, SO_2R^2, SO_3H, $S(NR^2R^7)R^2$, $S(O)(NR^2R^7)R^2$, NR^2R^7, aryl, heteroaryl or optionally substituted allyl, arylmethyl, alkynyl or alkenyl, where R^2, R^7 and R^8 have the definitions given above;

X is CH_2, O, S or NR^7, where R^7 has the definition given above;

R^{20} is a C_1-C_6 alkyl or an optionally substituted allyl, arylmethyl, alkenyl, aryl or heteroaryl;

R^{21} is hydrogen, a C_1-C_4 alkyl or optionally substituted allyl, arylmethyl, aryl or heteroaryl;

R^{30} and R^{31} each independently are hydrogen, a C_1-C_6 alkyl or an optionally substituted allyl, arylmethyl, aryl or heteroaryl, or R^{30} and R^{31} taken together can form a three- to seven-membered ring optionally substituted with hydrogen, F, Cl, OR^2 or NR^2R^7, where R^2 and R^7 have the definitions given above;

the wavy line in the compounds of formulas VII, XII and XIII represent an olefin bond in either the cis or trans configuration; and

the dotted lines in the structures depict optional double bonds.

Claims 24 - 27 depend from claim 23 and are directed to various embodiments thereof.

ANALYSIS

As directed to claims 41-55, the rejection is moot in light of the cancellation of claims 41-55 herein. As directed to claims 1-25, Applicant respectfully traverses the rejection.

The Examiner alleges that the instant compounds of Formula II and pharmaceutical compositions including compounds of Formula II are encompassed by compounds of Formula VII of U.S. Patent No. 5,693,646 (the '646 patent) and pharmaceutical compositions including compounds of Formula VII when R^{12} and R^{14} of Formula VII of the '646 patent are fluorine. Applicant respectfully submits that the test for obviousness-type double patenting is whether the claims at issue embrace the prior patent compounds, **not** whether the compounds of the prior patent encompass the compounds of the instant claims. In this instance, the claims at issue do not encompass the claims of the '646 patent. Applicant respectfully submits that, even

though there is overlap, there are compounds of Formula VII of the '646 patent that are not encompassed by the instant claims.

Independent claim 1 in the '646 patent recites compounds of Formulae VII, XII or XIII, having various substituents as defined in the claim. For example, the compounds of claim 1 of the '646 patent include substituents at position 5 represented by R^{20}, which is selected from among a C_1-C_6 alkyl or an optionally substituted allyl, arylmethyl, alkenyl, aryl or heteroaryl.

Independent claim 1 in the instant application recites compounds of Formulae I or II, having a double bond between positions 3 and 4, and having as substituents 2 methyl groups at position 2, a methyl substituent at position 4, a fluorine substituent at position 7 and position 9, hydrogen substituents at positions 8 and 10-12 and substituents at position 5 represented by R^8, which is selected from among C_1-C_{12} alkyl, C_1-C_{12} heteroalkyl, C_1-C_{12} haloalkyl, C_2-C_{12} alkenyl, C_2-C_{12} heteroalkenyl, C_2-C_{12} haloalkenyl, C_2-C_{12} alkynyl, C_2-C_{12} heteroalkynyl, C_2-C_{12} haloalkynyl, aryl and heteroaryl optionally substituted with one or more substituents independently selected from among hydrogen, C_1-C_4 alkyl, F, Cl, Br, I, CN, NO_2, NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SCH_3, OH, OCH_3, OCF_3, CF_3, $C(O)CH_3$, CO_2CH_3, $C(O)NH_2$, OR^{10}, SR^{10}, and $NR^{10}R^{11}$, where R^{10} and R^{11} each independently is hydrogen or C_1-C_4 alkyl.

Thus, when comparing the compounds as instantly claimed to the compounds of the '646 patent, there are compounds of Formula VII of the '646 patent that are not encompassed by the instant claims. For example, the claims of the '646 patent include substituents at position 5, such as, *e.g.*, optionally substituted allyl, that the instant claims do not recite. Therefore, the instant claims do not encompass the issued claims of the '646 patent.

Furthermore, the issued patent claims do not suggest a modification that would result in the instant claims. None of claims 1-27 of the '646 patent suggest a compound of Formula VII of the '646 patent with fluorine at position 7 and position 9. None of claims 1-27 of the '646 patent suggest a compound of Formula VII of the '646 patent with a double bond between positions 3 and 4 and substituted at positions 2 and 4 with methyl groups, at position 7 and 9 with fluorine, and at positions 8 and 10-12 with hydrogen.

Instant claims 2-14 ultimately depend from claim 1 and include every limitation thereof. Independent claim 15 is directed to a pharmaceutical composition that includes a pharmaceutically acceptable carrier and a compound of Formulae I or II, as discussed above. Claims 16-25 depend from claim 15 and are directed to various embodiments thereof.

Thus, because the instant claims do not encompass the claims of the '646 patent and none of the claims in the '646 patent suggest any modification that would have produced the

claimed compounds in the instant application, as between claims 1-27 in U.S. Patent No. 5,693,646 and pending claims 1-25, obviousness-type double patenting does not exist.

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In view of the above, reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,

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